Prehistory and History of Arabidopsis Research

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The earliest non-taxonomic appearance of Arabidopsis in the literature of botany appears to be a paper by Alexander Braun in 1873, describing a mutant plant found in a field near Berlin (7). The mutation was almost certainly in the *AGAMOUS* gene, now well known as one of the floral ABC regulators and cloned in 1990 (54). The next notable appearance of Arabidopsis in the experimental literature was in 1907, when Friedrich Laibach (1885–1967), a student in Strasburger's laboratory in Bonn, published an account of the chromosome number of several plants. He was attempting to find a plant with a small number of large chromosomes to be used in experiments to determine the individuality of chromosomes (23). Arabidopsis was not such a plant: the chromosomes are very small. The next relevant appearance of Arabidopsis was in a 1935 paper that resulted from a Russian expedition to find a plant that could be used in genetics and cytogenetics, as *Drosophila* was then used (15, 51). Although the small chromosome number (incorrectly stated by Titova to be a haploid no. of three; Laibach had correctly counted five in 1907) and rapid time to flowering were considered useful features, the small size of the plant and its parts were considered a disadvantage, as was the inability to distinguish different chromosome pairs. It does not appear that Arabidopsis was ever used in the laboratory by Titova and her colleagues.

Arabidopsis crops up again as a subject for laboratory investigation in 1943 when Laibach described the early results of studies in which he showed the short generation time, fecundity, ease of crosses, and the possibility of mutagenesis, and on this basis proposed adoption of Arabidopsis as a genetic model organism (24). The detailed results of the Laibach laboratory's studies on x-ray mutagenesis, which led to the first collection of Arabidopsis mutants, were published as a Ph.D. thesis by Laibach's student Erna Reinholz. The full publication of her 1945 thesis was, in fact, by the U.S. military: it seems that the thesis, with the word "Röntgen-Mutationen" in the title, came to the attention of those looking for a German atomic bomb program. It was published in 1947 as an unclassified captured document of the Joint Intelligence Objectives Agency (46).

There are reports through the 1950s and 1960s of the creation of mutants (25) and mutant collections (34, 35), of methods for generation of embryo lethals, and use of such methods to assess mutagenicity of chemicals (40, 44), and of use of the plant for controlled-environment studies and quantitative genetics (26, 27), but surprisingly little use was made of what is now such a central organism for laboratory work on flowering plants. There were the first stirrings of organization: A newsletter called *Arabidopsis Information Service* was founded in 1964 (publication continued until 1990). The original advisory board was F. Laibach, A. Müller, G. Rédei, and J. Veleminsky, with G. Röbbelen of the University of Göttingen serving as editor. Starting with the 1974 issue, the position of editor was taken by Albert Kranz of the University of Frankfurt. Two International Congresses of Arabidopsis were held before the molecular biology era: the first in Göttingen in April, 1965 (Fig. 1) and the second in Frankfurt am Main in September of 1976 (Fig. 2). Laibach and his students continued their Arabidopsis work by collecting a large number of ecotypes, which after their organization by Albert Kranz, formed the basis for the current ecotype collection (22).

The widespread adoption of Arabidopsis as a model plant, followed by the current revolution in plant genetics, physiology, and molecular genetics, occurred in the 1980s (Fig. 3). The idea that plant biologists should concentrate on a model organism was then under intense discussion, and a number of proposals were made such as using petunia because of its ease of transformation and the availability of haploid lines, or using tomato because of the availability of mutants (e.g. 42). Use of Arabidopsis for genetic experiments in plant physiology, in particular for finding auxotrophic mutations, had been proposed by George Rédei in 1975, in an article in the *Annual Review of Genetics* that brought Arabidopsis to the attention of many young geneticists and soon-to-be molecular cloners (45). What swung the balance in favor of Arabidopsis is not certain, though several contributions can be pointed out. One was the demonstration that mutational analysis can be done to saturation in laboratory conditions, and therefore that informative mutations in any gene could be obtained in screens of a practicable size (48, 49). Another was the demonstration that Arabidopsis has a very small genome and is therefore convenient for gene cloning, which at that time was difficult for large-genome organisms (28, 43); yet another was

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Figure 1. First International Symposium on Arabidopsis Research in Göttingen, April 21–24, 1965 (after the International Congress of Genetics in Scheweningen, and in honor of Laibach's 80th birthday). Left to right, first row: G. Röbbelen, S. Walles, I. Barthelmess, J. Veleminsky, ?, ?, A.D. McKelvie, ?, ?, and J. Bouharmont. Second row: G.P. Rédei, J.A.M. Brown, F. Laibach, E. Reinholz, T. Gichner, ?, B. Berger, and K. Napp-Zinn. Third row, J. Langridge, J. H.van der Veen, A. Müller, A.R. Kranz, ?, M. Jacobs, ?, ?, W.J. Feenstra, F. Schwanitz, ?, and F.J. Kribben. A ? indicates that the name of the individual is unknown. Copies of this photo courtesy of G.P. Rédei and A.R. Kranz.

the demonstration that Arabidopsis could be transformed with exogenous DNA (1, 29). These discoveries followed the publication of the first complete linkage map of Arabidopsis, which, along with the genome size data, showed that the relation between centimorgans and kilobases would permit straightforward map-based cloning, and showed clearly that morphological, life cycle, and hormone mutations were easily obtained (21). In addition, it was clear from even earlier work that embryo lethals could be produced and studied in detail (40, 36), and that Arabidopsis could be used as a model system for genetic analysis of plant embryo development (36).

A summary of the reasons to adopt Arabidopsis as a model system for plant development, physiology, and molecular genetics was published in *Science* in 1985 (38), another adding the possibility for complete mutant screens in *Trends in Genetics* in 1986 (14), and another with more emphasis on developmental mutations in 1987 (37). The first gene sequences were published in 1986 (10), and T-DNA-mediated transformation of Arabidopsis was also first established in 1986 (1, 29). This was followed by the first restriction fragment-length polymorphism map in 1988 (8), T-DNA insertional cloning (16, 30), map-based cloning (18, 2), and the extremely efficient vacuum infiltration method of transformation (5). Each method was developed to solve specific biological problems, and each added to the reasons to use Arabidopsis in the laboratory. The list of reasons to use Arabidopsis thus grew from the intrinsic properties of the plant such as small size, large seed number, and small genome to include experimentally derived properties such as ease of mutagenesis and transformation. Complete and free sharing of experimental protocols and material was established as the norm, further motivating researchers to use the organism.

The widespread adoption of Arabidopsis as a laboratory model system in plant biology has led to additional meetings; the 11th International Conference on Arabidopsis Research was held this summer, and the now-annual meetings have an attendance of nearly 1,000. These meetings, in addition to stock centers from which wild-type and mutant seed, as well as specific cDNA clones, genomic clones, DNA, and seed of T-DNA mutagenized pools are freely available, and a public internet-based database of sequence, clone, and mutant data add to the derived experimental properties, a set of derived social properties of the plant that further increases its value as an experimental system.

Concentration on the Arabidopsis model genetic system has brought to plant biology a fusion of classical and molecular genetics with plant development, plant physiology, and plant pathology. This has in turn led to our first mechanistic understanding of the

Figure 2. Second International Symposium on Arabidopsis Research in Frankfurt am Main, September 13–15, 1976. From left to right: front row, Gräf, Acedo, Venketeswaran, and Kranz. Second row, Demchenko, Scheidemann, Doddema, and Gresshof. Third row, Schweizer, Corcos, Negrutiu, D'Souza, and Sopory. Back row, Ledoux, Ratcliffe, Ambros, Maliga, Matigne, Jacobs, Feenstra, Rédei, Napp-Zinn, and Gomez-Campo. Copies of this photo courtesy of Ioan Negrutiu and Albert R. Kranz.

information transfer and cellular processes that regulate plant life—a first glimpse at how plants really work at the molecular level. Some (among many) areas where application of Arabidopsis genetics to the problems of plant biology has led to answers to longstanding questions include cell morphogenesis (19), root development (53), floral induction (3), flower and fruit development (47, 17), plant light perception (20), plant disease resistance (32, 13), plant cold and freezing resistance (50), and plant hormone action (31).

One comparison that helps to explain the revolution in plant biology stemming from Arabidopsis research is a comparison of the genetic versus the physiological ways of thinking. Prior to the fusion of genetics via Arabidopsis with plant physiology, plant physiologists were concerned with the flow and movement of substances in plants. Although this is still a fundamental concern in physiology (just think water), genetics added to this the view of organisms as flows of information as well as substances. The original concern of genetics was the flow of the information for development from one generation to the next. In the last 50 years, however, the informational view of life has expanded to include flow of information into cells (via ligands for receptors), flow from the cell surface to the nucleus via signal transduction cascades, and flow from the nucleus to the cytoplasm via mRNA and nuclear protein transit. Before Arabidopsis genetics and molecular genetics was applied, for example, to understanding ethylene as a plant hormone, the experiments in this field were largely on the effects of ethylene treatment on plants and cells, and on how and under what conditions ethylene is synthesized. Application of genetic methods to find Arabidopsis mutations that blocked information flow via ethylene (6) led to the other half of the field as we now know it—the nature of the receptors (9), the molecules in the signal transduction pathway, and the nuclear transcription factors that interact with the genes activated by ethylene in different cells (33). We now think of the hormone as a carrier of information that transmutes through a series of different biochemical forms, from a gas to a series of phosphorylated cytoplasmic proteins to nuclear DNA-binding proteins—a rather different view than that before genetics came to plant physiology.

A similar comparison of plant development before and after Arabidopsis can be made by reference to studies in plant responses to light. A recent history of this field makes exactly the point that Arabidopsis genetics has allowed a transition from studies of physiological response to light, to a mechanistic model of information transfer, described in terms of regulatory pathways (52). Another example of the change in viewpoint from physiological to physiological and genetic is in consideration of plant cell

Figure 3. Arabidopsis molecular biologists at Keystone, Colorado, 1985. Left to right, S. Somerville, C. Somerville, E. Meyerowitz, D. Meinke, M. Crouch, and M. Koornneef (see 41). Photo courtesy of Maarten Koornneef.

biology; this shift and the central role of Arabidopsis genetics in it has also been reviewed recently (11).

It is worth emphasizing that the change in plant biology brought by research on Arabidopsis has been conceptual as well as methodological. Flower development and its mechanisms were under study, and floral development mutants were available for more than a century before Arabidopsis came into the field. However, until genetical thinking came to plant biology, no double mutants of floral development genes were made. The experiments that led to our present models of flower development (12) could have been completed with *Antirrhinum* mutants available in the 1930s (39). The methods to do the work were not lacking in the 1930s, but the concepts of developmental genetics, of plant and animal life as a process of information flow from the genome that results in cellular differentiation, were not developed and applied to plants until much later. Thus experiments that now seem obvious were not done.

The most recent methodological breakthrough, and perhaps a precursor to the next stage in the evolution of our concept of plants, is the completion of the DNA sequencing of the Arabidopsis genome. We now know much of the information content of a plant cell, though in a highly encoded fashion. The information that is immediately accessible is the estimated sequence of 25,000 proteins. These include not only the functional recipes for plant life, but also important aspects of evolutionary history, thus forming a resource for future analysis. As almost one-half of the proteins indicated so far are unrelated to any protein with a known function, we can for the first time quantify our ignorance and browse a list of what we don't know. This in itself is a grand stimulus to curiosity-driven research. Additional structural information may soon follow: Electron tomography methods are approaching the resolution where entire cells may soon be described at the atomic level (4), expression data on each of the genes will no doubt accumulate, and the existing large collections of gene knockouts will eventually allow us to know the phenotypes of loss- and gain-of-function of all of the genes. To know what experiments to do next will not come automatically, however, our concept of plant life must continue to evolve. To use the new information productively we have to continue using specific tests of specific hypotheses to address such fundamental questions as how plants grow, how plant cells function and communicate with their neighbors, how plants sense and respond to their environments, and how plants change over evolutionary time.

ACKNOWLEDGMENTS

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CORRECTIONS

Vol. 124: 935–939, 2000

Schopfer, C.R., and Nasrallah, J.B. Self-Incompatibility. Prospects for a Novel Putative Peptide-Signaling Molecule.

Figure 2 was erroneously printed in black and white. Figure 2 has been reprinted in color on p 2204.

Vol. 124: 1007–1017, 2000

Stotz, H.U., Pittendrigh, B.R., Kroymann, J., Weniger, K., Fritsche, J., Bauke, A., and Mitchell-Olds, T. Induced Plant Defense Responses against Chewing Insects. Ethylene Signaling Reduces Resistance of Arabidopsis against Egyptian Cotton Worm But Not Diamondback Moth.

The GenBank accession number of the β-glucosidase gene was not included when this article was first published. The GenBank accession number is AJ251301.

Vol. 124: 1511–1514, 2000

Dennison, K.L., and Spalding, E.P. Glutamate-Gated Calcium Fluxes in Arabidopsis.

Figure 1 was erroneously printed in black and white in the original publication and again in Vol. 125 on p 1151. Figure 1 has been reprinted in color on p 2205.

Vol. 124: 1532–1539, 2000

Gibson, S.I. Plant Sugar-Response Pathways. Part of a Complex Regulatory Web.

In Table I, the line "*sis5* Is allelic to *aba4*" should have appeared as "*sis5* Is allelic to *abi4*." Table I has been reprinted on p 2206.

Vol. 125: 15–19, 2001

Meyerowitz, E.M. Prehistory and History of Arabidopsis Research.

Professor Georges Bernier of the Universite de Liege (Belgium) kindly sent the following corrections for the photographs that appeared as Figures 1 and 2. In Figure 1, the last person on the right of the first row is Silvano Bonotto, not J. Bouharmont; in the third row, between A.R. Kranz and M. Jacobs, the unidentified person is J. Bouharmont. In Figure 2, in the back row, the person identified as Matigne is in fact R. Matagne. We welcome any additional information on the names of those who appear in the photographs.

Vol. 125: 329–338, 2001

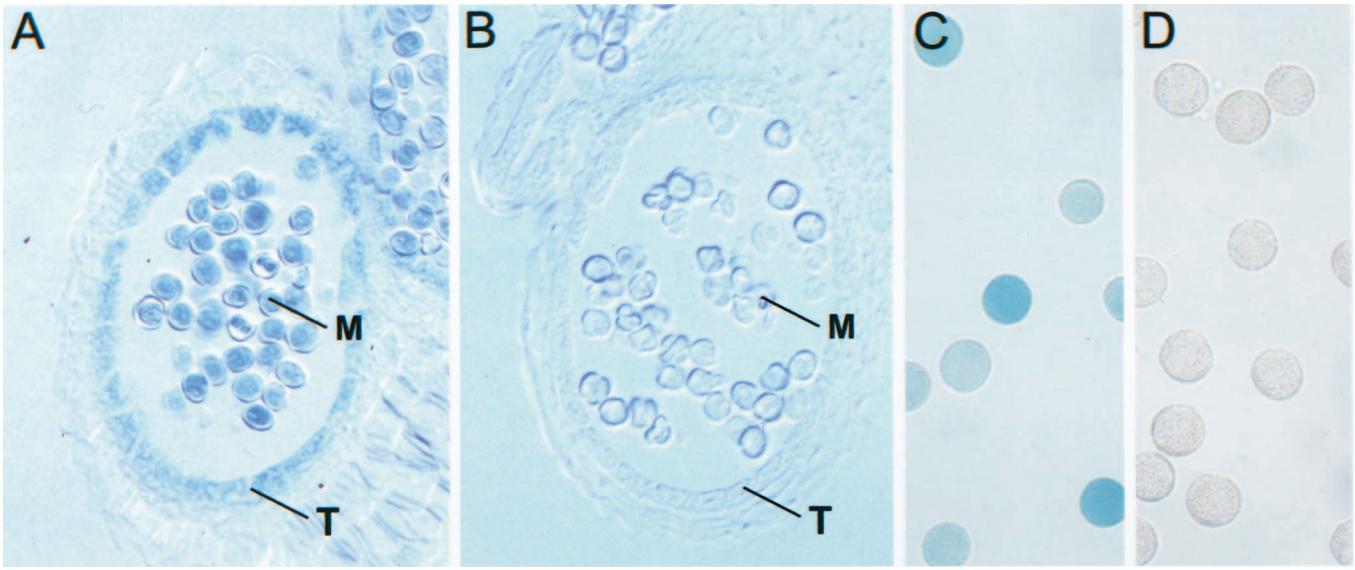
Taylor, A.R., and Assmann, S.M. Apparent Absence of a Redox Requirement for Blue Light Activation of Pump Current in Broad Bean Guard Cells.

Figures 2, 3, and 4 were not printed in the correct order. The correctly numbered figures with legends are reprinted on pp 2207–2209.

Acknowledgment

Vol. 125: No. 1, ii, 2001

We would like to acknowledge Jan Zeevaart, who supplied the photograph of the morning glory flower that appears on the cover of the January 2001 75th Anniversary Special Issue.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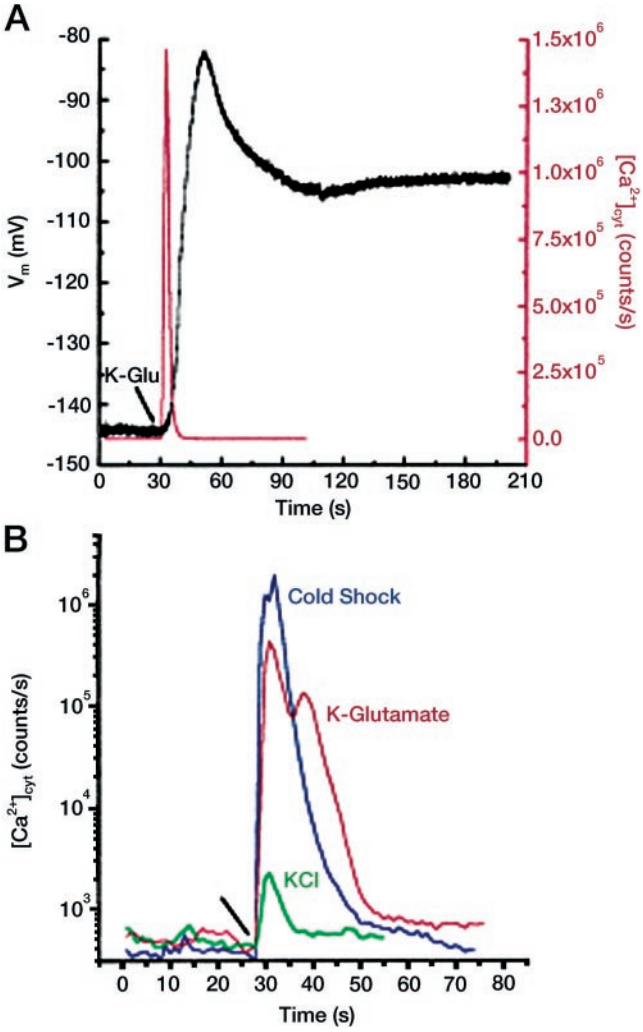
A
-80
-90
-100
-110
-120
-130
-140
-150
V_m (mV)
K-Glu
0
30
60
90
120
150
180
210
Time (s)
1.5x10^6
1.3x10^6
1.0x10^6
7.5x10^5
5.0x10^5
2.5x10^5
0.0
$[Ca^{2+}]_{cyt}$ (counts/s)
B
10^6
10^5
10^4
10^3
$[Ca^{2+}]_{cyt}$ (counts/s)
Cold Shock
K-Glutamate
KCl
0
10
20
30
40
50
60
70
80
Time (s)

Table I. *Sugar-response mutants and corresponding loci*

Mutants	Originals Selection	Loci	References
rsr	Reduced sensitivity to Suc induction of patatin expression		Martin et al., 1997
lba	Reduced sensitivity to Suc induction of β-amylase expression		Mita et al., 1997b
hba	Increased sensitivity to Suc induction of β-amylase expression		Mita et al., 1997a
sun	Reduced sensitivity to Suc repression of plastocyanin expression	*sun6* ls allelic to *abi4*	Dijkwel et al., 1997; Huijser ete al., 2000
sis	Reduced sensitivity to Glc or Suc-mediated inhibition of early seedling development	*sis1* ls allelic to *ctr1* *sis4* ls allelic to *aba2* *sis5* ls allelic to *abi4*	Laby et al., 2000; S. Gibson, R. Laby, and D. Kim, unpublished data
gin	Reduced sensitivity to Glc-mediated inhibition of early seedling development	*gin1* ls allelic to *aba2* *gin6* ls allelic to *abi4*	Zhou et al., 1998; Arenas-Huertero et al., 2000; J. Sheen, personal communication
prl	Increased sensitivity to sugar-mediated inhibition of early seedling development	*PRL1* Encodes a WD-40 protein	Németh et al., 1998; Bhalerao et al., 1999

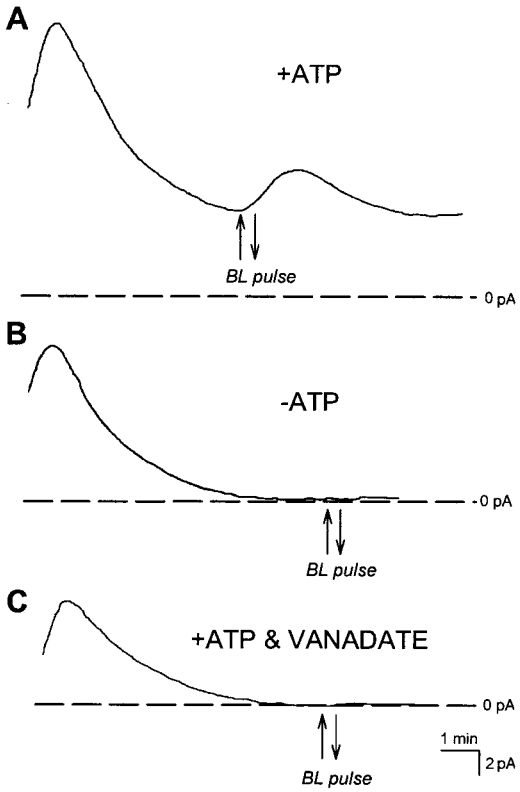

Figure 2. Steady-state- and BL-stimulated pump currents require ATP and are inhibited by vanadate. A, A typical recording with 5 mM ATP in the pipette under saturating RL. The cell responded to a 30-s pulse of BL with a typical transient increase in pump current. B, When ATP is absent from the pipette, cell currents quickly decay to 0 pA under saturating RL and are unresponsive to a pulse of BL. C, Inclusion of ATP and 20 μM vanadate in the pipette causes inhibition of pump current. All cells where pump current was inhibited by vanadate were unresponsive to BL pulses.

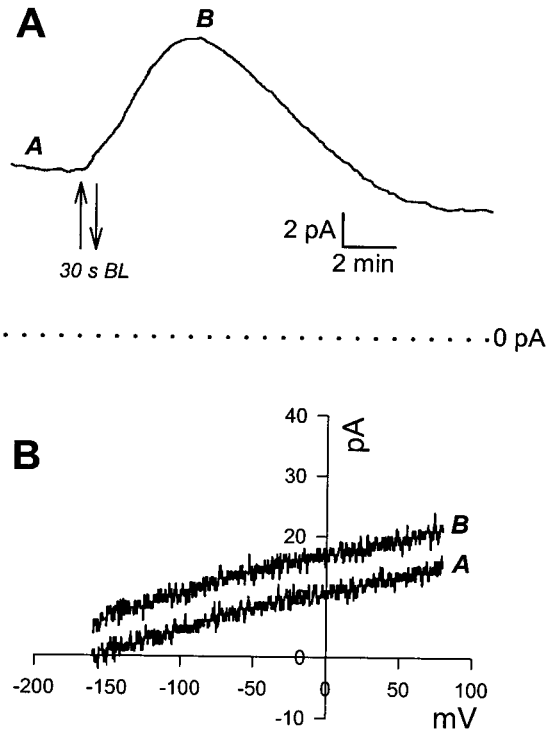

Figure 3. H^+-ATPase activation by a pulse of BL. Saturating RL background illumination was switched on before the beginning of the trace. A, Once stable baseline current is achieved a pulse of BL causes a transient increase in pump current. B, I/V ramps conducted before (*A*) and at the peak (*B*) of the response in A show the parallel shunt in pump current.

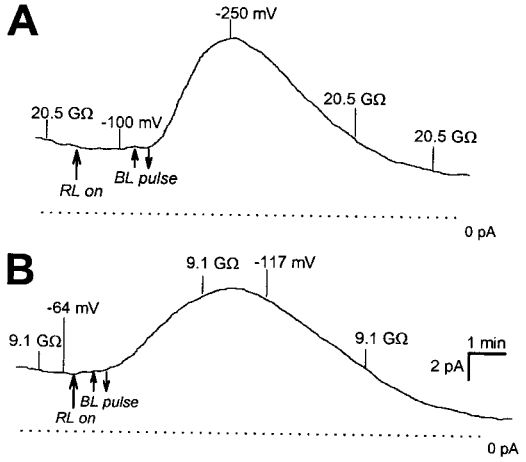

Figure 4. The effect of plasma membrane H^+-ATPase currents on membrane potential. The two traces show the pump current measured with ATP in the pipette. Membrane potential and input resistance are indicated on the traces at steady state and during BL-activated stimulation of pump current. Note the insensitivity to saturating RL illumination.